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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/803,459	03/19/2004	Arieh Gertler	28758.74	6294

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EXAMINER	
DANG, IAN D	
ART UNIT	**PAPER NUMBER**
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/803,459	GERTLER ET AL.	
	Examiner	Art Unit	
	Ian Dang	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-14 and 16-21* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 21* is/are withdrawn from consideration.

5)☒ Claim(s) *6, 8-10, 12-14, and 16-20* is/are allowed.

6)☒ Claim(s) *11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-6,8-14 and 16-21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03/19/2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the amendment and response filed on 01/15/2007. Claims 1-5, and 21 have been withdrawn as a non-elected invention. Claims 7 and 15 have been cancelled and claims 6 and 14 have been amended.

This application contains claims 1-5 and 21 drawn to an invention nonelected with traverse in the response of 11 September 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 6, 8-14, and 16-20 are pending and under examination.

Rejection Withdrawn

35 USC § 103

The rejection of claims 6-20 under 35 U.S.C. 103 has been withdrawn in view of the cancellation of claims 7 and 15 and Applicant's persuasive arguments (see pages 4-7 of the response mailed 01/15/2007).

Rejection Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) a method for detecting a level of free leptin comprising contacting a sample with a chicken leptin receptor domain of SEQ ID NO: 8 and (2) a kit for an assay of a

level of free leptin in a sample from a human and ovine comprising a chicken leptin receptor domain of SEQ ID NO: 8, does not reasonably provide enablement for a method for detecting a level of free leptin in a sample from an individual, who has a condition or a disease related to the level of free leptin in the sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

(ii) At page 7 of the response, Applicants allege that the specification describes the relevance of free leptin to conditions and diseases known in the art. Leptin has been found to exist mainly in the free form in obese individuals, but in the bound form in lean individuals (see the Description of the Related Art, third paragraph, and Janeckova, Physiol. Res. 50:443 (2001), page 444, second column, second full paragraph). Persons with inactivating mutations of the leptin receptor are morbidly obese, remain prepubertal, and have hypogonadotrophic hypogonadism (see Mantzoros, Ann. Intern. Med. 130:671 (1999), page 674, second column, first-third paragraphs). Accordingly, the determination of free leptin levels would be of significant value in diagnostic and therapeutic applications related to leptin physiology.

Applicant's arguments have been fully considered but are not found persuasive. The Examiner agrees with Applicants that free leptin levels are found in obese patients as recited the review by Janeckova. The art is unambiguous regarding the presence of free leptin in obese patients. However, many leptin related diseases, such as hypogonadotrophic or hypogonadism (see Mantzoros), are caused by mutations in the receptors inhibiting the leptin receptor signaling pathway and free leptin levels have not been correlated with these diseases.

In addition, Janeckova (2001) recites that leptin circulates in the plasma as a free form or bound to leptin-binding proteins. These plasma leptin-binding proteins have not yet been

identified, but are likely to include a soluble form of the leptin receptor (page 444, right column, 2nd full paragraph). In the review by Mantzoros (1999) and Janeckova (2001), the art is silent regarding free leptin levels in leptin relating diseases or conditions because it may be difficult to distinguish between the free form of leptin from the bound form of leptin.

Moreover, Applicants have not provided support for any other diseases related with to the level of free leptin. The invention is drawn to a method of detecting level of free leptin in a sample form an individual with a condition or a disease related to the level of free leptin in the sample. The invention is broad is large because the condition or a disease condition related to the level of free leptin encompasses a large number of diseases. For instance, Janeckova (2001) teach the administration of a GnRH agonist to women undergoing in vitro fertilization treatment increased leptin levels. The elevation of leptin levels was not coupled with an increase in BMI and thus was not the result of increased body fat mass. This indicates that other factors are also important in the regulation of leptin (page 446, right column, 2nd paragraph). In another instance, Janeckova (2001) recite that leptin may be physiological regulator of bone mass, and thus may be the link between amenorrhea and ostepenia (page 449, right column, last line of 1st full paragraph). Thus the reference by Janeckova teaches that leptin is directly or indirectly involved in numerous types of diseases.

Furthermore, leptin levels may not be predictable for the diagnosis a disease without providing identifying the characteristics of the population affected by the diseases. For instance, Janeckova (2001) teach that the significance of the leptin effect in the pathogenesis of obesity, anorexia nervosa, insulin resistance, hypertension and the polycystic ovary syndrome must be examined in various populations and under various experimental conditions (page 451, right column, last paragraph). Thus, each disease has varying levels of free leptin associated with the disease.

In view of the state or the art and the specification, free leptin levels are not predictable for a leptin related disease.

(iii) At page 7 of the response, Applicants argue that compliance with 35 USC 112, first paragraph, does not turn on whether an example is disclosed; an example may be working or prophetic. A working example is not required for enablement if the invention is disclosed in such a manner that one skilled in the art may practice it without an undue amount of experimentation. The present specification describes evidence present in the relevant art that indicates that free leptin has an important role in conditions and diseases related to leptin physiology. Therefore, one skilled in the art would have a reasonable expectation that free leptin levels would be linked to such conditions and diseases, and that free leptin levels in serum samples would be associated with a disorder or pathological condition related to leptin metabolism.

Applicant's arguments have been fully considered but are not found persuasive. Although Applicant is not required to provide examples of all embodiments of a claimed invention, Applicants must provide sufficient supporting evidence for the claimed invention. The presence of a working example is one factor among the 8 Wands factors necessary to fulfill the enablement requirement. However, with limited guidance and working examples in conjunction with consideration of the other 7 factors, Applicants have not provided sufficient evidence to make and use the claimed invention. The disclosure of the instant specification does not provide sufficient guidance to make/use the invention without undue experimentation.

In addition, the claimed invention requires undue experimentation because the art indicates that leptin levels are still not predictable for a disease in all populations. While free leptin levels may be indicative of a certain disease in some instances, free leptin levels may not have any roles in other diseases in other instances. For instance, free leptin levels correlate well with obese patients, but the link is not well established for other disorders, since further

studies need to investigate whether leptin is the link between amenorrhea and ostepenia. Without providing guidance or examples how to identify a population characteristics, it would required undue experimentation to make or use the invention.

Conclusion

Claim 11 is not allowed and claims 6, 8-10, 12-14, 16-20 are free of the art.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian Dang whose telephone number is (571) 272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ian Dang
Patent Examiner
Art Unit 1647
March 28,2007

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER